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**Characterization and Biomarker Analyses of Post-COVID-19 Complications and Neurological Manifestations.**

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**Public Summary:**

It was the purpose of this exploratory study to evaluate peripheral markers of inflammation associated with neurological dysfunction plus nEV cargo to explain the post-COVID-19 neurocognitive symptoms in the early stage of post-COVID-19 recovery.

**Scientific Abstract:**

As the SARS-CoV-2 pandemic continues, reports have demonstrated neurologic sequelae following COVID-19 recovery. Mechanisms to explain long-term neurological sequelae are unknown and need to be identified. Plasma from 24 individuals recovering from COVID-19 at 1 to 3 months after initial infection were collected for cytokine and antibody levels and neuronal-enriched extracellular vesicle (nEV) protein cargo analyses. Plasma cytokine IL-4 was increased in all COVID-19 participants. Volunteers with self-reported neurological problems (nCoV, n = 8) had a positive correlation of IL6 with age or severity of the sequelae, at least one co-morbidity and increased SARS-CoV-2 antibody compared to those COVID-19 individuals without neurological issues (CoV, n = 16). Protein markers of neuronal dysfunction including amyloid beta, neurofilament light, neurogranin, total tau, and p-T181-tau were all significantly increased in the nEVs of all participants recovering from COVID-19 compared to historic controls. This study suggests ongoing peripheral and neuroinflammation after COVID-19 infection that may influence neurological sequelae by altering nEV proteins. Individuals recovering from COVID-19 may have occult neural damage while those with demonstrative neurological symptoms additionally had more severe infection. Longitudinal studies to monitor plasma biomarkers and nEV cargo are warranted to assess persistent neurodegeneration and systemic effects.

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